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No.	• 1			Application Number	10/70:	5.282		/
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(3			First Named Inventor		Chackalamannil			
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	Express Abandonment Request Information Disclosure Statement			CD, Number of CD(s) Landscape Table on CID		PTO Form 1449 (3 pages); References (53 documents); Post Card		
	Certified Copy of Priority Document(s) Reply to Missing Parts/ Incomplete Application Reply to Missing Parts under 37 CFR 1.52 or 1.53			ks				
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Date		June 08, 2005			Reg. No.	43,04	1	
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Chackalamannil, S., et.al.

Group Art Unit: 1625

Application No.: 10/705,282

Examiner: To Be Assigned

Filed:

November 10, 2003

Attorney Docket No. : CV01185K1X

For:

Methods of Use of

Thrombin Receptor Antagonists

INFORMATION DISCLOSURE STATEMENT

Commissione P.O. Box 145 Alexandria, V	iO	
Sir:		
he above-ide applications, Application Nobelieved to h	sted on entified copy(ie lo(s) <u>10</u> nave rea	ant to the duty of disclosure under 37 C.F.R. § 1.56, it is requested that the the accompanying Form PTO-1449 be considered and made of record in patent application. Other than cited U.S. patents and published patent es) of these documents are enclosed were filed in related U.S. D/705,282 filed November 10,2003, respectively. Since the Examiner is ady access to the cited U.S. patents and published patent applications, ments are not herewith transmitted, but will be provided upon request.
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Dated: June 8, 2005 Schering-Plough Corporation Patent Department, K-6-1, 1990 2000 Galloping Hill Road Kenilworth, NJ 07033-0530 Facsimile No.: (908) 298-5388

By:

Gerard E. Reinhardt Reg. No.: 43,041
Attorney of Record
Telephone No.: (908) 298-2960

Respectfully submitted,

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OE VC,	Effective on 12			Complete if Known
	Fees pursuant to the Consolidated App		Application Number	10/705,282
O' BEET	FEE TRAN	Filing Date	11/10/2003	
UH O	For FY	2005	First Named Inventor	Chackalamannil
1 111.	Applicant deimonandi antitus	Examiner Name	To Be Assigned	
PATENT & TRADE	Applicant claims small entity s	Tatus. See 37 CFR 1.27	Art Unit	1625
	TOTAL AMOUNT OF PAYMENT	(\$) 180.00	Attorney Docket No.	CV01185K1X

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METHOD OF PAYMENT (check all that apply)						
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FEE CALCULATION						
1. BASIC FILING, SEA	RCH, AND EXAMINATION FILING FEES	FEES SEARCH FEES	EXAMINATION	FEES		
Application Typ	Fee (\$)	Fee (\$)	Fee (\$)	Fees Paid (\$)		
utility	300	500	200			
Design	200	100	130			
Plant	200	300	160			
Reissue	300	500	600			
Provisional	200	0	0			
2. EXCESS CLAIM FEES Fee Description Fee (\$)						
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3. APPLICATION SIZE FEE If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$250 (\$125 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41 (a)(1)(G) and 37 CFR 1. 16(s). Total Sheets Extra Sheets Number of each additional 50 or fraction thereof Fee (\$) Fee Paid (\$)						
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4. OTHER FEE(S) Non-English Specification, \$130 fee (no small entity discount) Fees Pald (\$)						
Other (e.g., late filing surcharge): Information Disclosure Statement						

SUBMITTED BY	, // / // //	-	
Signature	and & KirrloMAH	Registration No. (Attorney/Agent) 43,041	Telephone 908-298-2960
Name (Print/Type	Gerard E. Reinhardt		Date June 08, 2005

This collection of information is required by 37 CFR 1.136. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

ATTY, DOCKET NO.: CV01185K1X

SERIAL NO.: 10/705,282

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

APPLICANT: Chackalamannil, S.

FILING DATE:

GROUP: 1625

(Use several sheets if necessary)

11/10/2003 **U.S. PATENT DOCUMENTS** EXAMINER DOCUMENT DATE NAME CLASS SUB-FILING DATE IF **INITIAL** APPROPRIATE NUMBER CLASS 6,063,847 AA 05/16/00 AB 6,326,380 B1 12/04/01 AC 6,645,987 11/11/03 AD 6.894.065 05/17/05 AE 03/0216437 11/20/03 FOREIGN PATENT DOCUMENTS TRANSLATION DOCUMENT DATE COUNTRY SUB-CLASS **CLASS** NUMBER YES NO WO/9926943 A 06/03/99 AF AG WO/0196330 A 12/20/01 06/05/05 AH Invitation to pay additional fees ΑI AJ OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.) Ahn, Ho-Sam, et.al. "Development of proteinase-activated receptor 1 antagonists as therapeutic agents for thrombosis, restenosis and inflammatory diseases", CURRENT PHARMACEUTICAL DESIGN, Vol. 9 (28) pp. 2349 - 2365, (2003). Asanuma, Kunihiro, et.al. "Thrombin Inhibitor, Argatroban, Prevents Tumor Cell Migration and AL Bone Metastasis", ONCOLOGY, Vol. 67(2), pp. 166 – 173, (2004). Asokananthan, Nithiananthan, et.al. "Activation of protease-activated receptor (PAR)-1, PAR-2, AM and PAR-4 stimulates IL-6, IL-8, and prostaglandin E2 release from human respiratory epithelial cells", JOURNAL OF IMMUNOLOGY, Vol. 168 (7), pp. 3577 - 3585, (2002). Barrios, Victor, et.al. "Proteinase-activated receptor-2 mediates hyperresponsiveness in isolated guinea pig bronchi.", BIOCHEMICAL PHARMACOLOGY, Vol. 66 (3), pp. 519-525, (2003). AN Buresi, M.C., et.al. "Protease-activated receptor-1 stimulates Ca2+-dependent CI- secretion in AO human intestinal epithelial cells", AMERICAN JOURNAL OF PHYSIOLOGY- GASTRO INTEST LIVER PHYSIOL Vol. 281 (2, Pt. 1), G323-G332, (2001) Copple, Bryan, L., et. al. "Thrombin and protease-activated receptor-1 agonists promote AP lipopolysaccharide-induced hepatocellular injury in perfused livers", JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THÉRAPEUTICS, Vol. 305 (2), pp. 417 – 425, (2003) AQ Chambers, R.C.,et.al. "Coagulation cascade proteases and tissue fibrosis", BIOCHEMICAL SOCIETY TRANSACTIONS, Vol. 30 (2), pp. 194 - 200, (2002). AR Chambers, R.C., "Proteinase-activated receptors and the pathophysiology of pulmonary fibrosis", DRUG DEVELOPMENT RESEARCH, Vol. 60(1), pp. 29-35, (2003). Coughlin, S., et.al. "PARticipation in inflammation, JOURNAL OF CLINICAL INVESTIGATION, AS 111(1), pp. 25-27, (2003). D'Andrea, M. et.al., "Expression of protease-activated receptor-1, -2, -3, and -4 in control and experimentally inflamed mouse bladder", AMERICAN JOURNAL OF PATHOLOGY, Vol. 162(3), pp. 907-923, (2003). Darmoul, Dalila, et.al., "Activation of proteinase-activated receptor 1 promotes human colon cancer cell proliferation through epidermal growth factor receptor transactivation", MOLECULAR CANCER RESEARCH, Vol. 2(9), pp. 514-522, (2004). Derian, Claudia, et.al., "Therapeutic potential of protease-activated receptor-1 antagonists. Expert Opinion on Investigational Drugs Vol. 12(2), 209-221, (2003). Even-Ram, Sharona, et. al., "The pattern of expression of protease-activated receptors (PARs) during early trophoblast development", JOURNAL OF PATHOLOGY, Vol. 200(1), pp. 47-52,

	AX	Even-Ram, Sharona, et. al., "Tumor cell invasion is promoted by activation of protease activated receptor-1 in cooperation with the ανβ5 integrin", JOURNAL OF BIOLOGICAL CHEMISTRY, Vol. 276(14), pp.10952-10962, (2001).
,	AY	Feistritzer, Clemens, et.al., "Thrombin Affects Eosinophil Migration via Protease-Activated Receptor-1", INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, Vol. 135 (1),
 	AZ	12-16, (2004). Ferroni, P., et.al., "Platelet activation in type 2 diabetes mellitus" JOURNAL OF THROMBOSIS AND HAEMOSTASIS Vol. 2(8), pp. 1282-1291, (2004).
E	ВА	Flynn, A.N., et.al., "Proteinase-activated receptor 1 (PAR-1) and cell apoptosis" APOPTOSIS, Vol. 9(6), pp. 729-737, (2004).
E	ВВ	Fiorucci, Stefano, et.al., "PAR1 antagonism protects against experimental liver fibrosis.Role of proteinase receptors in stellate cell activation" HEPATOLOGY, Vol. 39(2), pp. 365-375 (2004).
E	ВС	Fortini, Mark, "PAR-1 for the course of neurodegeneration" CELL Vol. 116(5), pp. 631-632, (2004).
E	BD	Gabazza, Esteban C, "Progress in the understanding of protease-activated receptors", INTERNATIONAL JOURNAL OF HEMATOLOGY, Vol. 79(2), pp.117-122, (2004).
E	BE	Gaca, Marianna, et.al. "Regulation of hepatic stellate cell proliferation and collagen synthesis by proteinase-activated receptors" JOURNAL OF HEPATOLOGY, Vol. 36(3), pp. 362-369, (2002).
E	BF	Hauck, R.W, et.al. "Alpha-Thrombin stimulates contraction of human bronchial rings by activation of protease-activated receptors" AMERICAN JOURNAL OF PHYSIOLOGY, Vol. 277(1, Pt. 1), L22-L29, (1999).
E	3G	Howell, D.C.,et.al. "Direct thrombin inhibition reduces lung collagen, accumulation, and connective tissue growth factor mRNA levels in bleomycin-induced pulmonary fibrosis" AMERICAN JOURNAL OF PATHOLOGY Vol. 159(4), pp. 1383-95, (2001).
E	3H	Jin, Enjing, et.al. "Protease-activated receptor (PAR)-1 and PAR-2 participate in the cell growth of alveolar capillary endothelium in primary lung adenocarcinomas". CANCER Vol. 97(3), pp. 703-713. (2003).
	ВІ	Jurasz, Paul, et.al. "Platelet-cancer interactions: Mechanisms and pharmacology of tumour cell-induced platelet aggregation" BRITISH JOURNAL OF PHARMACOLOGY, Vol. 143(7), pp. 819-826, (2004).
E	3J	Kawabata, Atsufumi "Gastrointestinal functions of proteinase-activated receptors" LIFE SCIENCES, Vol. 74(2-3), pp. 247-254, (2003).
	3K	Kuroda, Ryotaro, et.al. "Pain information pathways from the periphery to the cerebral cortex" Yakugaku Zasshi, Vol. 123(7), pp. 533-546, (2003).
	3L	Lan, Rommel, et.al. "Altered expression and in vivo lung function of protease-activated receptors during influenza A virus infection in mice" AMERICAN JOURNAL OF PHYSIOLOGY: LUNG CELLULAR AND MOLECULAR PHYSIOLOGY, Vol. 286(2), L388-98, (2004).
В	ВМ	Liu, Jian, et.al. "Expression of functional protease-activated receptor 1 in human prostate cancer cell lines" UROLOGICAL RESEARCH Vol. 31(3), pp. 163-168, (2003).
		Liu, Y., et.al. "Expression of protease-activated receptor 1 in oral squamous cell carcinoma" CANCER LETTERS Vol. 169(2), pp. 173-180, (2001).
8	30	Moffatt, James, et.al. "Effects of inhaled thrombin receptor agonists in mice" British Journal of Pharmacology Vol. 143(2), pp. 269-275 (2004).
E	3P	Miyata, Satoshi, et.al. "Trypsin stimulates integrin α5β1-dependent adhesion to fibronectin and proliferation of human gastric carcinoma cells through activation of proteinase-activated receptor-2" JOURNAL OF BIOLOGICAL CHEMISTRY Vol. 275(7), pp. 4592-4598, (2000).
	3Q	Nierodzik, M. L., et.al. "Protease-activated receptor 1 (PAR-1) is required and rate-limiting for thrombin-enhanced experimental pulmonary metastasis" BLOOD Vol. 92(10), pp. 3694-700, (1998).
В	3R	Rattenholl, Anke, et.al. "Role of proteinase-activated receptors in cutaneous biology and disease" DRUG DEVELOPMENT RESEARCH Vol. 59(4), pp. 408-416, (2003).
В	38	Reed, Charles, et. al. "The role of protease activation of inflammation in allergic respiratory diseases" JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, Vol. 114(5), 997-1008, (2004).
		Reiter, Rosemarie, et.al. "Regulation of protease-activated receptor I (PAR1) on platelets and responsiveness to thrombin receptor activating peptide (TRAP) during systemic inflammation in humans" THROMBOSIS AND HAEMOSTASIS Vol. 90(5), 898-903 (2003).
В	3U	Robey, R.B., et.al. "Thrombin is a novel regulator of hexokinase activity in mesangial cells" KIDNEY INTERNATIONAL Vol. 57(6), pp. 2308-18. Journal code: 0323470, (2000)
B	3V	Roche, Nicholas, et. al. "Effect of acute and chronic inflammatory stimuli on expression of protease-activated receptors 1 and 2 alveolar macrophages. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY Vol. 111(2), pp. 367-373, (2003).

Bvv	Neurodegeneration, and Neuroprotection: Thrombin as Signaling Molecule in the Brain", THE NEUROSCIENTIST, Vol 10 (6), pp. 501 – 512, (2004).
BX	
BY	Sekiguchi, Fumiko, et.al. "Protease-activated receptors (PARs) as therapeutic targets: Development of agonists/antagonists and modulation of gastrointestinal functions" DRUG DESIGN REVIEWS – Online Vol. 1(4), pp. 287-296, (2004).
BZ	Shi, Xiaoli, et.al. "Protease-activated receptors (PAR1 and PAR2) contribute to tumor cell motility and metastasis" MOLECULAR CANCER RESEARCH Vol. 2(7), 395-402, (2004).
CA	Shimizu, Tadamichi, et.al. "Macrophage Migration Inhibitory Factor Is Induced by Thrombin and Factor Xa in Endothelial Cells" JOURNAL OF BIOLOGICAL CHEMISTRY Vol. 279(14), pp. 13729-13737, (2004).
СВ	Thamboo, T. P., et. al. "Hep Par 1 expression in carcinoma of the cervix: Implications for diagnosis and prognosis" JOURNAL OF CLINICAL PATHOLOGY Vol. 57(1), 48-53, (2004).
cc	Tran, Thai, et. al. "Protease-activated receptor (PAR)-independent growth and pro-inflammatory actions of thrombin on human cultured airway smooth muscle" British Journal of Pharmacology 138(5), 865-875, (2003).
CD	Vergnolle, Nathalie, et.al. "A role for proteinase-activated receptor-1 in inflammatory bowel diseases", JOURNAL OF CLINICAL INVESTIGATION Vol. 114(10), 1444-56 (2004).
CE	Villari, D., et.al. "Hep Par 1 in gastric and bowel carcinomas: an immunohistochemical study" PATHOLOGY Vol. 34(5), pp. 423-426, (2002).
CF	Wang, Junru, et.al. "Deficiency of microvascular thrombomodulin and up-regulation of protease-activated receptor-1 in irradiated rat intestine: Possible link between endothelial dysfunction and chronic radiation fibrosis" AMERICAN JOURNAL OF PATHOLOGY Vol. 160(6), 2063-2072, (2002).
CG	activation. FASEB JOURNAL Vol. 17(2), pp. 163-174, (2003).
СН	Yuan Ta Chun, et.al. "Protease-activated receptor 1: a role in prostate cancer metastasis" CLINICAL PROSTATE CANCER Vol. 3(3), pp. 189-91, (2004).
CI	Zhang, Xin, et.al. "Correlation of Protease-Activated Receptor-1 With Differentiation Markers in Squamous Cell Carcinoma of the Head and Neck and Its Implication in Lymph Node Metastasis. CLINICAL CANCER RESEARCH Vol. 10(24), pp. 8451-8459, (2004).
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